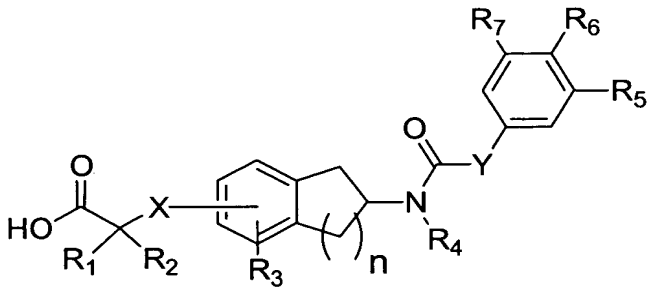
CLAIMS

1. A compound of Formula I



Formula I

or a pharmaceutically acceptable salt, C $_{1-6}$ ester or C $_{1-6}$ amide thereof, wherein

each of R_1 and R_2 is independently H, C $_{1-6}$ alkyl, $(CH_2)_mNR_aR_b$, $(CH_2)_mOR_8$, $(CH_2)_mNH(CO)R_8$, or $(CH_2)_mCO_2R_8$, where each of R_a, R_b, and R_8 is independently H or C $_{1-6}$ alkyl, or R_1 and R_2 taken together with the carbon atom to which they are attached are a C $_{3-7}$ cycloalkyl;

m is between 1 and 6;

n is 1 or 2;

X is O or S; wherein X is at the 5 or 6 position when n is 1; and wherein X is at the 6 or 7 position when n is 2;

R_3 is H, phenyl, C $_{1-3}$ alkoxy, C $_{1-3}$ alkylthio, halo, cyano, C $_{1-6}$ alkyl, nitro, NR_9R_{10}, $NHCOR_{10}$, $CONHR_{10}$; and $COOR_{10}$; and R_3 is ortho or meta to X;

R_4 is H or -(C $_{1-5}$ alkylene)R_{15}, where R_{15} is H, C_{1-7} alkyl, [di(C $_{1-2}$ alkyl)amino](C $_{1-6}$ alkylene), (C $_{1-3}$ alkoxyacyl)(C $_{1-6}$ alkylene), C $_{1-6}$ alkoxy, C $_{3-7}$ alkenyl, or C $_{3-8}$ alkynyl, wherein R_4 has no more than 9 carbon atoms; R_4 can

also be -(C_{1-5} alkylene)R_{15} wherein R_{15} is C_{3-6} cycloalkyl, phenyl, phenyl-O-, phenyl-S-, or a 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

Y is NH, NH-CH_2, and O;

each of R_5 and R_7 is independently selected from H, C_{1-6} alkyl, halo, cyano, nitro, COR_{11}, $COOR_{11}$, C_{1-4} alkoxy, C_{1-4} alkylthio, hydroxy, phenyl, $NR_{11}R_{12}$ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

R_6 is selected from C_{1-6} alkyl, halo, cyano, nitro, COR_{13}, $COOR_{13}$, C_{1-4} alkoxy, C_{1-4} alkylthio, hydroxy, phenyl, $NR_{13}R_{14}$ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

in addition, either R_5 and R_6 or R_6 and R_7 may be taken together to be a bivalent moiety, saturated or unsaturated, selected from $-(CH_2)_3-$, $-(CH_2)_4-$, and $(CH_{1-2})_pN(CH_{1-2})_q$,

p is 0-2 and q is 1-3, where the sum (p + q) is at least 2;

each of R_9 and R_{10} is independently C_{1-6} alkyl;
each of R_{11}, R_{12}, R_{13} and R_{14} is independently H or C_{1-6} alkyl;

wherein each of the above hydrocarbyl and heterocarbyl moieties may be substituted with between 1 and 3 substituents independently selected from F, Cl, Br, I, amino, methyl, ethyl, hydroxy, nitro, cyano, and methoxy.

2. A compound of claim 1, wherein one of R_1 and R_2 is methyl or ethyl.

3. A compound of claim 2, wherein each of R_1 and R_2 is methyl.

4. A compound of claim 1, wherein R_1 and R_2 taken together are cyclobutyl or cyclopentyl.

5. A compound of claim 1, wherein R_3 is H.

6. A compound of claim 1, wherein R_3 is C_{1-3} alkoxy, C_{1-3} alkylthio, halo, cyano, C_{1-6} alkyl, nitro, NR_9R_{10}, $NHCOR_{10}$, $CONHR_{10}$; or $COOR_{10}$.

7. A compound of claim 1, wherein R_4 is H or C_{2-7} alkyl.

8. A compound of claim 7, wherein R_4 is H or C_{2-5} alkyl.

9. A compound of claim 8, wherein R_4 is ethyl.

10. A compound of claim 8, wherein R_4 is H.

11. A compound of claim 1, wherein n is 1.

12. A compound of claim 1, wherein n is 2.

13. A compound of claim 1, wherein Y is $NH\text{-}CH_2$.

14. A compound of claim 1, wherein Y is NH.

15. A compound of claim 1, wherein X is S.

16. A compound of claim 1, wherein X is O.

17. A compound of claim 1, wherein at least one of R_5 and R_7 is H.

18. A compound of claim 17, wherein R_6 is C $_{1-4}$ alkyl, halomethoxy, halomethylthio, or di(C $_{1-3}$ alkyl)amino.

19. A compound of claim 18, wherein R_6 is trifluoromethoxy, difluoromethoxy, trifluoromethyl, trifluoromethylthio, t-butyl, isopropyl, or dimethylamino.

20. A compound of claim 3, wherein R_3 is H, R_4 is C $_{2-7}$ alkyl, and Y is NH.

21. A compound of claim 20, wherein X is S.

22. A compound of claim 20, wherein n is 1.

23. A compound of claim 20, wherein n is 2.

24. A compound of claim 20, wherein R_4 is C $_{2-5}$ alkyl.

25. A compound of claim 24, wherein R_4 is ethyl.

26. A compound of claim 20, wherein R_6 is trifluoromethoxy, difluoromethoxy, trifluoromethyl, trifluoromethylthio, t-butyl, isopropyl, or dimethylamino.

27. A compound of claim 1, wherein each of R_1 and R_2 is independently H, C $_{1-6}$ alkyl, $(CH_2)_mNR_aR_b$, or $(CH_2)_mOR_8$, where each of R_a, R_b, and R_8 is independently H or C $_{1-6}$ alkyl;

m is between 1 and 6;

n is 1 or 2;

X is O or S; wherein X is at the 5 or 6 position when n is 1; and wherein X is at the 6 or 7 position when n is 2;

R_3 is H, phenyl, C $_{1-3}$ alkoxy, C $_{1-3}$ alkylthio, halo, C $_{1-6}$ alkyl, or NR_9R_{10}, and R_3 is ortho or meta to X;

R_4 is H or -(C $_{1-5}$ alkylene)R_{15}, where R_{15} is H, C_{1-7} alkyl, [di(C $_{1-2}$ alkyl)amino](C $_{1-6}$ alkylene), (C $_{1-3}$ alkoxyacyl)(C $_{1-6}$ alkylene), C $_{1-6}$ alkoxy, or C $_{3-7}$ alkenyl, wherein R_4 has no more than 9 carbon atoms;
R_4 can also be -(C $_{1-5}$ alkylene)R_{15} wherein R_{15} is C $_{3-6}$ cycloalkyl, phenyl, phenyl-O-, phenyl-S-, or a 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

Y is NH or $NHCH_2$;

each of R_5 and R_7 is independently selected from H, C $_{1-6}$ alkyl, halo, COR_{11}, $COOR_{11}$, C $_{1-4}$ alkoxy, C $_{1-4}$ alkylthio, hydroxy, and $NR_{11}R_{12}$;

R_6 is selected from C $_{1-6}$ alkyl, halo, COR_{13}, $COOR_{13}$, C $_{1-4}$ alkoxy, C $_{1-4}$ alkylthio, phenyl, $NR_{13}R_{14}$ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

each of R_9 and R_{10} is independently C $_{1-6}$ alkyl;
each of R_{11}, R_{12}, R_{13} and R_{14} is independently H or C $_{1-6}$ alkyl;

wherein each of the above hydrocarbyl and heterocarbyl moieties may be substituted with between 1 and 3 substituents independently selected from F, Cl, amino, methyl, ethyl, hydroxy, and methoxy.

28. A compound of claim 1, selected from:
2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;
2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-pentyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{2-[1-Ethyl-3-(4-isopropylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-pentyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[3-(4-Dimethylaminophenyl)-1-ethylureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-(3-methylbutyl)-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-methylbutyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methy-2-{2-[1-pent-4-enyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-chloro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-bromo-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid; and

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-trifluoromethoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid.

29. A compound of claim 1, selected from

2-Methyl-2-{2-[1-hexyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid ;

2-{2-[3-(4-Dimethylaminophenyl)-1-pentylureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-Methyl-2-{2-[1-butyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-pentyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[3-(4-*tert*-Butylphenyl)-1-(3-pentyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-[2-(3-(Biphenyl-4-yl-1-pentylureido)indan-5-ylsulfanyl]-2-methylpropionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-hexyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-butyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-chloro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-bromo-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid; and

2-Methyl-2-{2-[1-hexyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid.

30. A compound of claim 1, selected from:

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[3-(4-Trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid; and

2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid.

31. A compound of claim 1, selected from:

2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid; and

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid.

32. A pharmaceutical composition, comprising a compound of claim 1, 20, 27, 28, 30, or 31.

33. A method for treating or inhibiting the progression of Syndrome X, said method comprising administering to a patient in need of treatment a pharmaceutically-effective amount of a composition comprising a compound of claim 1, 20, 27, 28 or 31.

34. A method of claim 33, wherein said Syndrome X is a combination of
(a) One or more conditions selected from impaired glucose tolerance, hyperinsulinemia, hyperglycemia, insulin resistance, and early, intermediate or late Type II diabetes (NIDDM), impaired fasting glucose tolerance, and complications thereof;
(b) Dyslipidemia
(c) Obesity or an overweight condition; and
(d) Hypertension.

35. A method of claim 33, wherein said Syndrome X is a combination of two or more conditions selected from (a).

36. A method of claim 33, wherein said compound is a first pharmaceutically active agent, and wherein said method further comprises the step of administering to the patient a jointly-effective amount of a second pharmaceutically active agent that is an anti-diabetic agent, a lipid lowering agent, or a blood-pressure lowering agent.

37. A method of claim 36, wherein said second agent is selected from insulin and PPAR alpha or PPAR gamma modulating agents.

38. A method of claim 36, further comprising the step of administering a jointly-effective amount of a third pharmaceutically active agent.

39. A method of claim 39, wherein said third pharmaceutically active agent is selected from an anti-diabetic agent, a lipid lowering agent, and a blood-pressure lowering agent.

40. A method for treating obesity or an overweight condition, said method comprising the step of administering to a patient a pharmaceutically effective amount of a composition comprising a compound of formula (I).

41. A method of claim 40, wherein said method is a method for treating dyslipidemia and either obesity or an overweight condition.

42. A method of claim 40, wherein said method is a method for treating obesity and a condition selected from Type II diabetes, insulin resistance, hyperglycemia, impaired glucose tolerance, and hyperinsulinemia.